

WHAT IS CLAIMED IS:

- 1 1. A method of diagnosing PAPA syndrome in a subject comprising detecting a mutation in
2 a gene allele of the subject, wherein the gene allele encodes CD2BP1.
- 1 2. The method of claim 1, wherein the mutation is within the region of the gene that
2 encodes from amino acid 122 to 288 inclusive in CD2BP1.
- 1 3. The method of claim 1, wherein the mutation includes a G748C transversion in a
2 CD2BP1 gene.
- 1 4. The method of claim 1, wherein the mutation includes a G688A transition in a CD2BP1
2 gene.
- 5 5. The method of claim 1, wherein the detection is by denaturing HPLC.
- 6 6. The method of claim 1, wherein the detection is by DNA sequence analysis.
- 7 7. A method of diagnosing PAPA Syndrome in a subject comprising identifying a single
nucleotide polymorphism (SNP) in the CD2BP1 gene of the subject, comprising:
 - 8 (a) obtaining a sample of nucleic acid from the subject; and
 - 9 (b) determining the identity of one or more SNPs in the CD2BP1 gene, wherein the
SNPs are located at nucleotides 688 and 748 of the CD2BP1 gene.
- 1 8. The method of claim 7, wherein the determining step comprises amplifying at least a
2 portion of a nucleic acid molecule encoding the CD2BP1 gene.
- 1 9. The method of claim 7, wherein the identity of one or more SNPs is determined by DNA
2 sequence analysis.
- 1 10. A method of screening for an agent that modifies an immune response in cells that
2 express a CD2BP1 with a mutation associated with PAPA syndrome, the method comprising:
 - 3 contacting the cells with an agent suspected of modifying the immune response;
 - 4 measuring an indicator of immune response; and
 - 5 comparing the measurement to the same immune response indicator in a control cell under
6 comparable conditions in the absence of the agent;
 - 7 wherein a difference in the indicator is indicative of an agent that modifies the immune response.
- 1 11. The method of claim 10, wherein the mutation is in the region of CD2BP1 bounded by
2 amino acids 122 to 288 inclusive.

- 1 12. The method of claim 10, wherein the cells express CD2BP1 with a G668A mutation as
2 numbered in SEQ ID NO:21.
- 1 13. The method of claim 10, wherein the cells express CD2BP1 with a G748C mutation as
2 numbered in SEQ ID NO:19.
- 1 14. The method of claim 10, wherein the mutation is in amino acid 250 of the CD2BP1.
- 1 15. The method of claim 10, wherein the mutation is an E250Q mutation of the CD2BP1.
- 1 16. The method of claim 10, wherein the mutation is in amino acid 230 of the CD2BP1.
- 1 17. The method of claim 10, wherein the mutation is an A230T mutation of the CD2BP1.
- 1 18. The method of claim 10, wherein the indicator is T-cell rosetting.
- 1 19. The method of claim 10, wherein the indicator is altered motility of the cells.
20. The method of claim 10, wherein the indicator is CD2 triggered adhesion involving
CD58.
21. The method of claim 10, wherein the indicator is integrin-mediated adhesion activated
through CD2 or a CD15 carrier.
22. The method of claim 21, wherein the CD15 carrier is CD66a.
23. A method of screening for an agent that modifies an immune response in cells that
express a mutant CD2BP1, wherein the mutant CD2BP1 comprises a A230T mutation or a
E250Q mutation, comprising:
- contacting the cells with an agent suspected of modifying the immune response;
- measuring an indicator of immune response; and
- comparing the measurement to the same immune response indicator in control cells under
comparable conditions in the absence of the agent;
- wherein a difference in the indicator is indicative of an agent that modifies the immune response.
- 1 24. The method of claim 23, wherein the indicator is T-cell rosetting.
- 1 25. The method of claim 23, wherein the indicator is altered motility of the cells.
- 1 26. The method of claim 23, wherein the indicator is CD2 triggered adhesion involving
2 CD58.
- 1 27. The method of claim 23, wherein the indicator is integrin-mediated adhesion activated
2 through CD2 or a CD15 carrier.
- 1 28. The method of claim 27, wherein the CD15 carrier is CD66a.

1 29. A method of screening for an agent that modifies an interaction of CD2BP1 with a binding
2 partner of CD2BP1, wherein the CD2BP1 has a mutation associated with PAPA syndrome, the
3 method comprising:

4 measuring the binding of the CD2BP1 to a binding partner in the presence of an agent
5 suspected of altering the binding interaction of the CD2BP1 and the binding partner and
6 comparing the binding in the presence of the agent to a measured control of the binding
7 interaction in the absence of the agent, wherein a difference in the binding interaction is
8 indicative of an effector of CD2BP1 binding to a binding partner.

1 30. The method of claim 29, wherein the binding partner is the cytoplasmic portion of CD2,
2 PTP PEST, PTP HSCF, WASP, pyrin, c-Abl, or a CD15 carrier.

1 31. The method of claim 29, wherein the mutation is in the region of CD2BP1 bounded by
2 amino acids 122 to 288 inclusive.

32. The method of claim 29, wherein the mutation is in amino acid 250 of the CD2BP1.

33. The method of claim 29, wherein the mutation is an E250Q mutation of the CD2BP1.

34. The method of claim 29, wherein the mutation is in amino acid 230 of the CD2BP1.

35. The method of claim 29, wherein the mutation is an A230T mutation of the CD2BP1.

36. A method of screening for an agent that modifies an interaction of mutant CD2BP1 with
a binding partner of CD2BP1, wherein the mutant CD2BP1 comprises an A230T mutation or an
E250Q mutation, the method comprising:

measuring the binding of the mutant CD2BP1 to a binding partner in the presence of an
agent suspected of altering the binding interaction of the mutant CD2BP1 and the binding
partner, and comparing the binding in the presence of the agent to a measured control of the
binding interaction in the absence of the agent, wherein a difference in the binding interaction is
indicative of an effector of mutant CD2BP1 binding to a binding partner.

1 37. The method of claim 36, wherein the binding partner is the cytoplasmic portion of CD2,
2 PTP PEST, PTP HSCF, WASP, pyrin, c-Abl, or a CD15 carrier.

1 38. An isolated nucleic acid molecule or the complement thereof, wherein the molecule
2 encodes an amino acid sequence comprising the sequence of SEQ ID NO:20 or SEQ ID NO:22,
3 with conservative amino acid substitutions.

1 39. The molecule of claim 38, wherein the molecule encodes an amino acid sequence
2 comprising the sequence of SEQ ID NO:20.

- 1 40. The molecule of claim 38, wherein the nucleic acid molecule comprises the nucleic acid
2 sequence of SEQ ID NO:19.
- 1 41. The molecule of claim 38, wherein the molecule encodes an amino acid sequence
2 comprising the sequence of SEQ ID NO:22.
- 1 42. The molecule of claim 38, wherein the nucleic acid molecule comprises the nucleic acid
2 sequence of SEQ ID NO:21.
- 1 43. An expression construct comprising the nucleic acid molecule of claim 38 operably
2 linked to an expression control sequence.
- 1 44. The expression construct of claim 43, further defined as a plasmid expression vector or a
2 viral expression vector.
- 1 45. A host cell transformed or transfected with the expression construct of claim 43, or a
2 progeny of the cell.
- 1 46. The host cell of claim 45, further defined as a bacterial cell, a mammalian cell, or a
2 human cell.
- 1 47. An isolated nucleic acid molecule comprising about 20 contiguous nucleotides of SEQ ID
2 NO:18, including: (a) nucleotide 688 wherein the G is replaced by an A; (b) nucleotide 748
3 wherein the G is replaced by a C; or both (a) and (b).
- 1 48. The isolated nucleic acid molecule of claim 47, wherein the nucleotide corresponding to
2 nucleotide 688 of SEQ ID NO:18 is located at the 5' end of the molecule.
- 1 49. The isolated nucleic acid molecule of claim 47, wherein the nucleotide corresponding to
2 nucleotide 688 of SEQ ID NO:18 is located at the 3' end of the molecule.
- 1 50. The isolated nucleic acid molecule of claim 47, wherein the nucleotide corresponding to
2 nucleotide 748 of SEQ ID NO:18 is located at the 5' end of the molecule.
- 1 51. The isolated nucleic acid molecule of claim 47, wherein the nucleotide corresponding to
2 nucleotide 748 of SEQ ID NO:18 is located at the 3' end of the molecule.
- 1 52. An isolated nucleic acid molecule comprising the complement of the nucleic acid
2 molecule of claim 47.
- 1 53. An array of nucleic acid molecules attached to a solid support, the array comprising an
2 oligonucleotide that will hybridize to the nucleic acid molecule of claim 47, under conditions in
3 which the oligonucleotide will not substantially hybridize to a nucleic acid molecule consisting
4 of SEQ ID NO:18.